QSAR PREDICTION OF N-OCTANOL/WATER PARTITION COEFFICIENT FOR POLYCHLORINATED BIPHENYLS

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ABSTRACT

The logarithmic n-octanol/water partition coefficient (logKow) is a very important property which concerns water-solubility, bioconcentration factor, toxicity and soil absorption coefficient of organic compounds. Quantitative structure–activity relationship (QSAR) model for logKow of 133 polychlorinated biphenyls (PCBs) is analyzed using multiple linear regression analysis (MLRA) followed by statistical evaluation by SPSS software (IBM). In order to indicate the influence of different molecular descriptors on logKow values and well understand the important structural factors affecting the experimental values, a set of physiochemical and topological parameters were taken into consideration. Three multivariable linear models derived from three groups of different molecular descriptors were built. Moreover, each molecular descriptor in these models was discussed to well understand the relationship between molecular structures and their logKow values. The proposed models gave the following results: the square of correlation coefficient, R^2, for the models with with one, two, three, four and five molecular descriptors are 0.8553, 0.9233, 0.9319, 0.9345 and 0.9455. Our results are much more superior then the result reported by Liu et al. Therefore simple 2D QSAR reported by us is much betters then the 3D QSAR modeling of Liu et al.

Keywords: - Polychlorinated biphenyls; Quantitative Structure Activity Relationship; SPSS.

I. INTRODUCTION

Polychlorinated biphenyls (PCBs) are persistent organic contaminants and widespread environmental pollutants; they were used in plastifiers formulation of coatings, inks, adhesives, flame retardants, pesticide extenders and in the micro-encapsulation of dyes for carbonless duplicating papers. Human exposure to PCBs occurs mainly from eating food that contains these chemicals *(Schecter et al., 2001; Erdogrul et al., 2005; Coelhan et al., 2006)*. It has been reported that meat, dairy products, and fish, makes up more than 90% of the intake of PCBs for the general population *(Schecter et al., 1997)*. PCBs are rapidly absorbed from the gastrointestinal tract, and are distributed and accumulated in the liver and adipose tissues. The compounds have serious ecologically harmful effects and are implicated as potent carcinogens. Thus, there is a need for prediction tools to study PCBs' properties including retention behavior, properties, and activity/toxicity for which analytical standards are currently difficult to obtain, but yet for which environmental data are needed. The logarithmic n-octanol/water partition coefficient (logKow) is an important property for pharmacology, toxicology and medicinal chemistry. There have been many reports on the prediction of logKow for PCBs, most of the reported prediction methods are based on thermodynamically oriented theories *(Banerjee and Howard, 1988)*,

connectivity indexes *(Randic, 1975; Sabljic et al., 1993)* and characteristic root index (CRI) *(Melek and Inel, 1995)*. Three-dimensional structure–activity correlations for prediction of thermodynamic properties of PCBs have been recently made to predict the enthalpy of vapourization and enthalpy of sublimation *(Puri et al., 2002)*. The octanol/water partition coefficient expressed as logKow is an important property for various applications in pharmacology, toxicology and medicinal chemistry *(Leo, 1993)*. logKow is used to model partitioning of chemicals between the lipophilic membrane and the relative hydrophobic cellular cytoplasmic material. logKow quantities hydrophobicity of chemicals and is important both for predicting pharmacokinetics and pharmacodynamics of drugs and toxicants *(Klopman et al., 1994)*. Lipophilicity is traditionally measured in the octanol/ water system. logKow values have been shown to be generally satisfactory for modelling protein binding and lipophilic interactions with biological membranes consisting largely of protein *(Platts et al., 1999)*. Several methods have been described in the literature for the estimation of the octanol/water partition coefficient, which is logKow *(Khadikar et al., 2002)*. Here, based on the octanol/water partition coefficient of 133 polychlorinated biphenyl (PCBs) congeners, we report a QSAR model by the MLRA method of 2D-QSAR technique. The purpose of the present study was to investigate the relationship between the octanol/water partition coefficient of 133 polychlorinated biphenyls (PCBs) and their molecular parameters. Moreover, molecular descriptors were discussed to explore the influence of structural features on the values of logKow. This paper provided a simple and straightforward way to predict the logKow values of PCBs from their structures and gave some insight into structural features related to the logKow values of the compounds. The prediction results are satisfactory in all the three groups. The software Chemscatch , Dragon , NCSS and SPSS has been applied successfully in a variety of QSAR analyses *(Oblak et al., 2000; Katritzky et al, 2001)*. It can calculate a comprehensive set of descriptors: Physicochemical parameters, constitutional descriptors, topological descriptors, geometrical descriptors, and connectivity indices (in this work, we calculated so many descriptors).

II. MATERIALS AND METHODS

2.1. Data Set

All data of the present investigation were obtained from the reference *(Mancang Liu et al., 2007)*. The data set for this investigation consisted of 133 PCBs.The geometry of biphenyl template is depicted along with atom numbering (Fig. 1).

2.2. Molecular Descriptor Generation

To obtain a QSAR model, compounds are often represented by the molecular descriptors. The calculation process of the molecular descriptors was described as below: The two-dimensional molecular structures of 133 PCBs were drawn by Chem Sketch 12.0 then calculated some parameters. Then this optimize structure files were exported into software Dragon 6.0 to calculate all kinds of descriptors. The software Dragon 6.0 can calculate Physicochemical parameters, constitutional, topological, geometrical, descriptors and has been successfully used in various QSAR researches.Then value of all parameters put into NCSS statistical and data analysis software or SPSS (We can also use MSTAT instead of SPSS & NCSS) statistical and data analysis software to get data regression and correlation. Constitutional descriptors are related to the number of atoms and bonds in each molecule. Topological descriptors include valence and non-valence molecular connectivity

indices calculated from the hydrogen-suppressed formula of the molecule, encoding information about the size, composition, and the degree of branching of a molecule. The topological descriptors describe the atomic connectivity in the molecule. The geometrical descriptors describe the size of the molecule and require 3D-coordinates of the atoms in the given molecule. The electrostatic descriptors reflect characteristics of the charge distribution of the molecule. The quantum chemical descriptors offer information about binding and formation energies, partial atom charge, dipole moment, and molecular orbital energy levels.

III. RESULTS AND DISCUSSION

By using the multiple linear regression analysis (MLRA) method of 2D-QSAR, regression models were developed for 133 PCBs. To select the sets of descriptors that are most relevant to logKow values and effectively show the relation between descriptors and logKow values of these compounds, five subsets with the descriptors from one to five were determined to establish the QSAR models. Multi-linear regression method for descriptor selection proceeds with a reselections of descriptors by sequentially eliminating descriptors which do not match any of the following criteria: (i) the F-test greater than one unit; (ii) R^2 value less than a value defined at the start (default 0.01); (iii) the student's t-test less than that defined (default 0.1); and (iv) duplicate descriptors having a higher squared inter-correlation coefficient than a predetermined level (usually 0.8). The next step involves correlation of the given property with (i) the top descriptor in the above list with each of the remaining descriptors, and (ii) the next one with each of the remaining descriptors, etc. The goodness of the correlation is tested by the correlation coefficient (R^2) and The stability of the correlations was tested against the cross-validated coefficient (R^2_{CV}). Besides, it will demonstrate which descriptors have bad or missing values, which descriptors are insignificant, and which descriptors are highly intercorelated .This information will be helpful in reducing the number of descriptors involved in the search for the best QSAR/QSPR model. Comparison with Mancang Liu result Liu et al in their result have reported R^2 for modeling with one, two and three molecular descriptors as 0.8854, 0.9239 and 0.9285 respectively. We have observed that in our case R^2 for models with one, two, three, four and five molecular descriptors are 0.8553, 0.9233, 0.9319, 0.9345 and 0.9455. Our results are much more superior then the result reported by Liu et al. Therefore simple 2D QSAR reported by us is much betters then the 3D QSAR modeling of Liu et al.

3.1 Best Mono-Parametric Model

When topological indices were taken as independent parameters ten mono-parametric models have been obtained the best model given below:-

$$\text{LogKow} = 0.1171(\pm 0.2222)2\chi + 0.1171$$

$$N = 133,\ Se = 0.0462,\ R^2 = 0.8553,\ \text{F-Ratio} = 774.4140,\ Q = 20.0178$$

The R^2 value comes out to be 0.8553 suggesting 85% variance.

3.2 Best Bi-Parametric Model

When two parameter are taken together then nine bi-parametric models have been obtained the best model contains J and 0χ. The R^2 value of best model is 0.9233. This model is given below:-

$$\text{LogKow} = -4.6094(\pm 0.3880)J\ 0.7532(\pm 0.0269)0\chi + 6.2647$$

$$N = 133,\ Se = 0.0338,\ R^2 = 0.9233,\ R^2A = 0.9222,\ \text{F-Ratio} = 782.9010,\ Q = 28.4285$$

In this model the coefficient of J is negative and 0χ is positive suggesting that high value of 0χ and low value of J is favored for LogKow. A significant improvement R^2 is seen.

3.3 Best Tri Parametric Model

When three parameter are taken together seven tri parametric models have been obtained with R^2 value from 0.9240 to 0.9319. Among these seven models the best model contains J, Jhetz and 0χ. The best model given below:-

LogKow= -20.2160(±3.9034)J 10.5965(±2.6386)Jhetz 0.4219(±0.0863)0χ +10.5793

N= 133, Se=0.0319, R^2=0.9319, R^2A=0.9309, F-Ratio=588.0490,Q=30.2617

In the above model J has negative coefficient and Jhetz and 0χ have positive coefficient suggesting that low value of J and high value of Jhetz and 0χ will favor the modeling of LogKow activity.

3.4 Best Tetra-Parametric Model

When four parameter are taken together five tetra-parametric models have been obtained with R^2 value 0.9345 for the best model. Among these five models the best model contains J, Jhetz, Jhete and 0χ. The best model given below:-

LogKow= -25.0014(±4.3736)J 10.0885(±2.6058)Jhetz 4.4862(±1.9610)Jhete 0.4160(±0.0850)0χ +9.5054

N=133, Se=0.0314, R^2=0.9345, R^2A=0.9325, F-Ratio=456.8190,Q=30.7864

In the above model J has negative coefficient and Jhetz, Jhete and 0χ have positive coefficient suggesting that low value of J and high value of Jhetz and 0χ will favor the modeling of LogKow activity.

3.5 Best Penta Parametric Model

When five parameter are taken together then penta parametric models have been obtained with R^2 value 0.9455.The best model contains J, Jhetz, Jhetm, Jhetp and 2χ. The best model given below:-

LogKow= -48.1522(±4.9569)J 33.6836(±3.9428)Jhetz -29.3426(±4.6428)Jhetm

31.2638(±5.1472)Jhetp 0.7679(±0.1179)2χ -0.3693

N= 133, Se=0.0288, R^2=0.9455, R^2A=0.9433, F-Ratio=440.3250,Q=33.7627

In the above model the coefficient of J, Jhetm has negative coefficient and Jhetz, Jhetp and 2χ have positive coefficient suggesting that low value of J, Jhetm and high value of Jhetz, Jhetp and 2χ will favor the modeling of LogKow activity. On the basis of Q value also for this penta-perametric model is the best model for the modeling of LogKow activity of compound under investigation. The predicted power of this model has been obtained by plotting a graph between observed and estimated LogKow values and comes out to be 0.9455 on the basis of cross validated statistics five parametric model is found to be best.

IV. CONCLUSION

A quantitative structure–activity relationship model was derived to study the logKow values of a diverse set of 133 PCBs. Five QSAR models were developed with the squared correlation coefficient (R^2) of one, two, three, four and five molecular descriptors are 0.8553, 0.9233, 0.9319, 0.9345 and 0.9455. These models showed strong predictive ability. Among all the descriptors, topological descriptors were found to have high coding capabilities for the logKow values and were selected to represent the chemical structures. The present work provides an effective method for the prediction of the logKow values for the PCBs. This study also showed that the utility of

the QSAR treatment involving descriptors derived solely from chemical structure and the correlation equation and descriptors can be used for the prediction of the logKow values for unknown structures.

Following conclusion may be drawn on the basis of above discussion.

(1.) Topological parameters are the best parameters for modeling LogKow activity of PCB derivatives.

(2.) 2D QSAR modeling using MLRA analysis has been found to be better than 3D QSAR modeling (HM method as reported by Liu et al.)

(3.) The best model suggests that for synthesizing new potent PCB chemicals. The structure having higher value of Jhetz, Jhetp and 2χ should be preferred.

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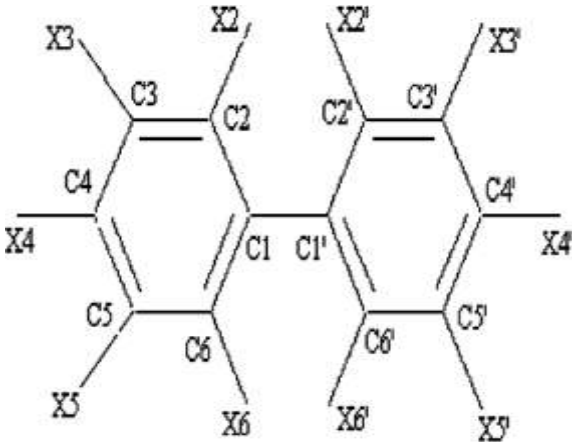
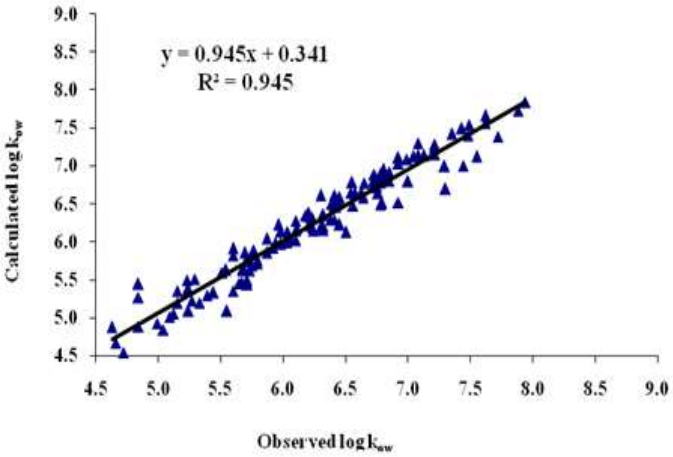


Fig.1 Geometry of biphenyl template with atom numbering



(Fig-2) Correlation between Observed and Calculated activity using best Penta Parameteric model (Table-3)

(Table- 1) Details Of Compounds With Their Activity Used In The Present Study.

COMPOUND NO.	COMPOUND NAME	EXPERIMENTAL Log Kow
1	3-Chlorobiphenyl	4.66
2	4-Chlorobiphenyl	4.63
3	2,2'-DiChlorobiphenyl	4.72
4	2,3-DiChlorobiphenyl	4.99
5	2,3'-DiIChlorobiphenyl	4.84
6	2,4-DiChlorobiphenyl	5.15
7	2,4'-DiChlorobiphenyl	5.09
8	3,3'-DiChlorobiphenyl	5.27
9	3,4-DiChlorobiphenyl	5.23
10	3,4'-DiChlorobiphenyl	5.15
11	4,4'-DiChlorobiphenyl	5.23
12	2,2',3-TriChlorobiphenyl	5.12
13	2,2',4-TriChlorobiphenyl	5.39
14	2,2',5-TriChlorobiphenyl	5.33
15	2,2',6-TriChlorobiphenyl	5.04
16	2,3,3'-TriChlorobiphenyl	5.6
17	2,3,4-TriChlorobiphenyl	5.68
18	2,3.4'-TriChlorobiphenyl	5.29
19	2,3,6- TriChlorobiphenyl	5.44
20	2,3',4- TriChlorobiphenyl	5.54
21	2,3',5- TriChlorobiphenyl	5.65
22	2,4,4'- TriChlorobiphenyl	5.71
23	2,4',5- TriChlorobiphenyl	5.68
24	2,4',6- TriChlorobiphenyl	5.24
25	2,3',4'- TriChlorobiphenyl	5.71
26	2,3',5'- TriChlorobiphenyl	5.71
27	2,2',3,3'- TetraChlorobiphenyl	5.67
28	2,2',3,4- TetraChlorobiphenyl	5.79
29	2,2',3,4'- TetraChlorobiphenyl	5.72
30	2,2',3,5'- TetraChlorobiphenyl	5.73

31	2,2',3,6- TetraChlorobiphenyl	4.84
32	2,2'3,6'- TetraChlorobiphenyl	4.84
33	2,2',4,4'- TetraChlorobiphenyl	5.94
34	2,2',4,5- TetraChlorobiphenyl	5.69
35	2,2',4,5'- TetraChlorobiphenyl	5.87
36	2,2',4,6- TetraChlorobiphenyl	5.75
37	2,2',4,6'- TetraChlorobiphenyl	5.51
38	2,2',5,5'- TetraChlorobiphenyl	5.79
39	2,2',5,6'- TetraChlorobiphenyl	5.55
40	2,2',6,6- TetraChlorobiphenyl	5.24
41	2,3,3',4- TetraChlorobiphenyl	6.1
42	2,3,4,4'- TetraChlorobiphenyl	6.24
43	2,3,4',5- TetraChlorobiphenyl	6.1
44	2,3,4',6- TetraChlorobiphenyl	5.76
45	2,3,5,6- TetraChlorobiphenyl	5.96
46	2,3',4,4'- TetraChlorobiphenyl	5.98
47	2,3',4,5- TetraChlorobiphenyl	6.32
48	2,3',4,6- TetraChlorobiphenyl	6.03
49	2,3',4,6- TetraChlorobiphenyl	5.76
50	2,4,4',5- TetraChlorobiphenyl	6.1
51	2,4,4',6- TetraChlorobiphenyl	6.03
52	2,3',4',5'- TetraChlorobiphenyl	5.98
53	2,2',3,3',6- PentaChlorobiphenyl	5.6
54	2,2',3,4,4'- PentaChlorobiphenyl	6.18
55	2,2',3,4,5- PentaChlorobiphenyl	6.38
56	2,2',3,4,5'- PentaChlorobiphenyl	6.23
57	2,2',3,4,6- PentaChlorobiphenyl	6.5
58	2,2',3,4,6'- PentaChlorobiphenyl	5.6
59	2,2',3,4',5- PentaChlorobiphenyl	6.32
60	2,2',3,4',6- PentaChlorobiphenyl	5.87
61	2,2',3,5,5'- PentaChlorobiphenyl	6.32
62	2,2',3,5,6- PentaChlorobiphenyl	6.06
63	2,2',3,5',6- PentaChlorobiphenyl	5.92
64	2,2',3,4',5'- PentaChlorobiphenyl	6.3
65	2,2',3,4',6'- PentaChlorobiphenyl	6.04
66	2,2',4,4',5- PentaChlorobiphenyl	6.41
67	2,2',4,4',6- PentaChlorobiphenyl	6.23
68	2,2',4,5',6- PentaChlorobiphenyl	6.11
69	2,3,3',4,4'- PentaChlorobiphenyl	6.79
70	2,3,3',4,5- PentaChlorobiphenyl	6.92
71	2,3,3',4',6- PentaChlorobiphenyl	6.2
72	2,3,3',5,6- PentaChlorobiphenyl	6.41
73	2,3,3',5',6- PentaChlorobiphenyl	6.45
74	2,3,4,4',5- PentaChlorobiphenyl	6.71
75	2,3,4,4',6- PentaChlorobiphenyl	6.44
76	2,3,4',5,6- PentaChlorobiphenyl	6.39
77	2,3',4,4',5- PentaChlorobiphenyl	6.57
78	2,3',4,4',6- PentaChlorobiphenyl	6.4
79	2,3',4,5,5'- PentaChlorobiphenyl	6.3
80	2,3',4,5',6- PentaChlorobiphenyl	6.42
81	2,3',4,4',5'- PentaChlorobiphenyl	6.64
82	2,2',3,3',4,5- HexaChlorobiphenyl	6.76

83	2,2',3,3',4,5'- HexaChlorobiphenyl	7.3
84	2,2',3,3',4,6- HexaChlorobiphenyl	6.78
85	2,2',3,3',4,6'- HexaChlorobiphenyl	6.2
86	2,2',3,3',5,6- HexaChlorobiphenyl	6.2
87	2,2',3,3',5,6'- HexaChlorobiphenyl	6.32
88	2,2',3,4,4',5- HexaChlorobiphenyl	6.82
89	2,2',3,4,4',5'- HexaChlorobiphenyl	6.73
90	2,2',3,4,4',6'- HexaChlorobiphenyl	6.58
91	2,2',3,4,5,5'- HexaChlorobiphenyl	6.75
92	2,2',3,4,5,6'- HexaChlorobiphenyl	6.56
93	2,2',3,4,5',6- HexaChlorobiphenyl	6.45
94	2,2',3,4',5,5'- HexaChlorobiphenyl	6.85
95	2,2',3,4',5',6- HexaChlorobiphenyl	6.41
96	2,2',3,5,5',6- HexaChlorobiphenyl	6.42
97	2,2',4,4',5,5'- HexaChlorobiphenyl	6.8
98	2,2',4,4',5,6'- HexaChlorobiphenyl	6.65
99	2,2',4,4',6,6'- HexaChlorobiphenyl	6.54
100	2,3,3',4,4',5- HexaChlorobiphenyl	7.44
101	2,3,3'4,4',6- HexaChlorobiphenyl	6.78
102	2,3,3',4',5,6- HexaChlorobiphenyl	6.78
103	2,3,3',4',5',6- HexaChlorobiphenyl	6.63
104	2,3,3',5,5',6- HexaChlorobiphenyl	7
105	2,3',4,4',5,5'- HexaChlorobiphenyl	7.29
106	3,3',4,4',5,5'- HexaChlorobiphenyl	7.55
107	2,2',3,3',4,4',5- HeptaChlorobiphenyl	7.08
108	2,2',3,3',4,5,5'- HeptaChlorobiphenyl	7.21
109	2,2',3,3',4,5,6'- HeptaChlorobiphenyl	6.85
110	2,2',3,3',4,5',6- HeptaChlorobiphenyl	6.92
111	2,2',3,3',4,6,6'- HeptaChlorobiphenyl	6.55
112	2,2',3,3',4,5',6'- HeptaChlorobiphenyl	6.73
113	2,2',3,3',5,5',6- HeptaChlorobiphenyl	6.85
114	2,2',3,3',5,6,6'- HeptaChlorobiphenyl	6.41
115	2,2',3,4,4',5,5'- HeptaChlorobiphenyl	7.21
116	2,2',3,4,4',5,6- HeptaChlorobiphenyl	7.13
117	2,2',3,4,4',5,6'- HeptaChlorobiphenyl	6.92
118	2,2',3,4,4',5',6- HeptaChlorobiphenyl	7.04
119	2,2',3,4,5,5',6- HeptaChlorobiphenyl	6.99
120	2,2',3,4',5,6,6'- HeptaChlorobiphenyl	6.78
121	2,3,3',4,4',5,5'- HeptaChlorobiphenyl	7.72
122	2,3,3',4,4',5,6- HeptaChlorobiphenyl	7.08
123	2,3,3',4,4',5',6- HeptaChlorobiphenyl	7.21
124	2,3,3',4,5,5',6- HeptaChlorobiphenyl	7.21
125	2,3,3',4',5,5',6- HeptaChlorobiphenyl	7.21
126	2,2',3,3',4,4',5,5'- OctaChlorobiphenyl	7.62
127	2,2',3,3',4,4',5,6- OctaChlorobiphenyl	7.35
128	2,2',3,3',4,4',5,6'- OctaChlorobiphenyl	7.43
129	2,2',3,4,4',5,5',6- OctaChlorobiphenyl	7.49
130	2,2',3,4,4',5,6,6'- OctaChlorobiphenyl	7.48
131	2,3,3',4,4',5,5',6- OctaChlorobiphenyl	7.62
132	2,2',3,3',4,4',5,5',6- NonaChlorobiphenyl	7.94
133	2,2',3,3',4,4',5,6,6'- NonaChlorobiphenyl	7.88

(Table-2) Cross Validated Values For Topological Parameters.

S.N.	Parameters used	PRESS	SSY	PRESS/SSY	R^2cv	PSE	S_{PRESS}
1.	2χ	10.9541	64.7563	0.1691	0.8309	0.2869	0.2936
2.	J, 0χ	5.8039	69.9065	0.0830	0.9170	0.2088	0.2137
3.	J, Jhetz, 0χ	5.1589	70.5515	0.0731	0.9268	0.1969	0.2015
4.	J, Jhetz, Jhete, 0χ	4.9563	70.7541	0.0700	0.9300	0.1930	0.1975
5.	J, Jhetz, Jhetm, Jhetp, 2χ	4.1291	71.5813	0.0576	0.9424	0.1761	0.1803

(Table- 3) Regression Parameters And Quality Of Correlation With Best Topological Parameters.

Model	Parameter used	Ai=(1……....5)	B	Se	R^2	R^2a	F Ratio	Q=R/Se
Mono Parameteric	2χ	0.1171(±0.2222)	0.1171	0.0462	0.8553	-	774.4140	20.0178
Di Parameteric	J 0χ	-4.6094(±0.3880) 0.7532(±0.0269)	6.2647	0.0338	0.9233	0.9222	782.9010	28.4285
Tri Parameteric	J Jhetz 0χ	-20.2160(±3.9034) 10.5965(±2.6386) 0.4219(±0.0863)	10.5793	0.0319	0.9319	0.9303	588.0490	30.2617
Tetra Parameteric	J Jhetz Jhete 0χ	-25.0014(±4.3736) 10.0885(±2.6058) 4.4862(±1.9610) 0.4160(±0.0850)	9.5054	0.0314	0.9345	0.9325	456.8190	30.7864
Penta Parameteric	J Jhetz Jhetm Jhetp 2χ	-48.1522(±4.9569) 33.6836(±3.9428) -29.3426(±4.6428) 31.2638(±5.1472) 0.7679(±0.1179)	-0.3693	0.0288	0.9455	0.9433	440.3250	33.7627

(Table-4) Observed And Calculated Activity For The Compounds Using Penta Parameteric Model (Table -3).

Comp. No.	Observed log kow	Calculated log kow	Residual
1	4.6600	4.6710	-0.0110
2	4.6300	4.8720	-0.2420
3	4.7200	4.5440	0.1760
4	4.9900	4.9260	0.0640
5	4.8400	4.8780	-0.0380
6	5.1500	5.1980	-0.0480
7	5.0900	5.0090	0.0810
8	5.2700	5.2260	0.0440

9	5.2300	5.3690	-0.1390
10	5.1500	5.3490	-0.1990
11	5.2300	5.4960	-0.2660
12	5.1200	5.0540	0.0660
13	5.3900	5.2970	0.0930
14	5.3300	5.1930	0.1370
15	5.0400	4.8380	0.2020
16	5.6000	5.3480	0.2520
17	5.6800	5.6170	0.0630
18	5.2900	5.5060	-0.2160
19	5.4400	5.3320	0.1080
20	5.5400	5.6300	-0.0900
21	5.6500	5.4540	0.1960
22	5.7100	5.7640	-0.0540
23	5.6800	5.6460	0.0340
24	5.2400	5.3820	-0.1420
25	5.7100	5.4830	0.2270
26	5.7100	5.4340	0.2760
27	5.6700	5.4640	0.2060
28	5.7900	5.7130	0.0770
29	5.7200	5.7390	-0.0190
30	5.7300	5.6230	0.1070
31	4.8400	5.4410	-0.6010
32	4.8400	5.2650	-0.4250
33	5.9400	5.9880	-0.0480
34	5.6900	5.8550	-0.1650
35	5.8700	5.8530	0.0170
36	5.7500	5.6830	0.0670
37	5.5100	5.5930	-0.0830
38	5.7900	5.7550	0.0350
39	5.5500	5.0900	0.4600
40	5.2400	5.0900	0.1500
41	6.1000	6.0150	0.0850
42	6.2400	6.1480	0.0920
43	6.1000	6.1490	-0.0490
44	5.7600	5.8920	-0.1320
45	5.9600	6.2220	-0.2620
46	5.9800	6.1330	-0.1530
47	6.3200	6.1560	0.1640
48	6.0300	5.9920	0.0380
49	5.7600	5.8530	-0.0930
50	6.1000	6.2760	-0.1760
51	6.0300	6.1340	-0.1040
52	5.9800	5.9700	0.0100
53	5.6000	5.8170	-0.2170
54	6.1800	6.3470	-0.1670
55	6.3800	6.2860	0.0940

56	6.2300	6.1880	0.0420
57	6.5000	6.1270	0.3730
58	5.6000	5.9110	-0.3110
59	6.3200	6.3470	-0.0270
60	5.8700	6.0380	-0.1680
61	6.3200	6.2040	0.1160
62	6.0600	6.0150	0.0450
63	5.9200	5.9190	0.0010
64	6.3000	6.1980	0.1020
65	6.0400	6.1040	-0.0640
66	6.4100	6.4650	-0.0550
67	6.2300	6.3180	-0.0880
68	6.1100	6.1770	-0.0670
69	6.7900	6.5070	0.2830
70	6.9200	6.5190	0.4010
71	6.2000	6.2170	-0.0170
72	6.4100	6.2870	0.1230
73	6.4500	6.2250	0.2250
74	6.7100	6.7170	-0.0070
75	6.4400	6.5450	-0.1050
76	6.3900	6.5020	-0.1120
77	6.5700	6.6280	-0.0580
78	6.4000	6.4850	-0.0850
79	6.3000	6.6090	-0.3090
80	6.4200	6.4580	-0.0380
81	6.6400	6.5810	0.0590
82	6.7600	6.6380	0.1220
83	7.3000	6.6920	0.6080
84	6.7800	6.4840	0.2960
85	6.2000	6.3840	-0.1840
86	6.2000	6.3330	-0.1330
87	6.3200	6.3550	-0.0350
88	6.8200	6.8580	-0.0380
89	6.7300	6.8080	-0.0780
90	6.5800	6.6300	-0.0500
91	6.7500	6.7320	0.0180
92	6.5600	6.4700	0.0900
93	6.4500	6.5780	-0.1280
94	6.8500	6.7990	0.0510
95	6.4100	6.5060	-0.0960
96	6.4200	6.4710	-0.0510
97	6.8000	6.9470	-0.1470
98	6.6500	6.7700	-0.1200
99	6.5400	6.6450	-0.1050
100	7.4400	6.9990	0.4410
101	6.7800	6.8960	-0.1160
102	6.7800	6.7800	0.0000

103	6.6300	6.6350	-0.0050
104	7.0000	6.7910	0.2090
105	7.2900	6.9930	0.2970
106	7.5500	7.1210	0.4290
107	7.0800	7.1320	-0.0520
108	7.2100	7.1490	0.0610
109	6.8500	6.9050	-0.0550
110	6.9200	7.0290	-0.1090
111	6.5500	6.7760	-0.2260
112	6.7300	6.8880	-0.1580
113	6.8500	6.8970	-0.0470
114	6.4100	6.6170	-0.2070
115	7.2100	7.2310	-0.0210
116	7.1300	7.1360	-0.0060
117	6.9200	7.1030	-0.1830
118	7.0400	7.1220	-0.0820
119	6.9900	7.0810	-0.0910
120	6.7800	6.8660	-0.0860
121	7.7200	7.3800	0.3400
122	7.0800	7.3000	-0.2200
123	7.2100	7.2520	-0.0420
124	7.2100	7.2800	-0.0700
125	7.2100	7.1570	0.0530
126	7.6200	7.5630	0.0570
127	7.3500	7.4200	-0.0700
128	7.4300	7.4920	-0.0620
129	7.4900	7.5360	-0.0460
130	7.4800	7.3980	0.0820
131	7.6200	7.6590	-0.0390
132	7.9400	7.8340	0.1060
133	7.8800	7.7250	0.1550

(Table-5) Correlation Matrix Showing Inter-Correlation Among All The Parameters With The Activity.

	logkow	**W**	**J**	**Jhetz**	**Jhetm**
logkow	1.0000				
W	0.8968	1.0000			
J	0.6795	0.7919	1.0000		
Jhetz	0.7531	0.8410	0.9933	1.0000	
Jhetm	0.7533	0.8417	0.9920	0.9992	1.0000
Jhetv	0.4659	0.5515	0.7064	0.7007	0.7012
Jhete	0.6986	0.8041	0.9975	0.9938	0.9925
Jhetp	0.6997	0.8078	0.9980	0.9950	0.9958
0χ	0.9166	0.9505	0.8868	0.9319	0.9327
1χ	0.9130	0.9505	0.8915	0.9355	0.9362